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10/658,873	09/05/2003	Michael S. Kopreski	00-1312-K	5207

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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,873	KOPRESKI, MICHAEL S.	
	Examiner	Art Unit	
	FRANK W. LU	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,8,9,12,14,17,18,20,23,25,28,29,45 and 46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 5, 8, 9, 12, 14, 17, 18, 20, 23, 25, 28, 29, 45, and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on September 23, 2009 has been entered. The claims pending in this application are claims 1, 4, 5, 8, 9, 12, 14, 17, 18, 20, 23, 25, 28, 29, 45, and 46. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of applicant's amendment filed on September 23, 2009.

Information Disclosure Statement

2. Since applicant has not provided legible copies of some references listing in the information disclosure statement filed on April 14, 2009, these references have not been considered and have been struck through (see attached 1449 forms).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 1 is rejected as vague and indefinite since the claim does not indicate how to correlate the detected amplified product and amount or concentration of said RNA species or cDNA therefrom. Please clarify.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 4, 5, 8, 9, 12, 20, 23, 45, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balazs *et al.,* (WO 90/09456, published on August 23, 1990) in view of Guin *et al*., (Biochemical Medicine, 13, 224-230, 1975) and Korneluk *et al.,* (US Patent No. 6,656,704, priority date: August 5, 1996).

Regarding claims 1 and 4, Balazs *et al.,* teach extracting total extracellular RNA from blood plasma or serum from a human (ie., a cancer patient), amplifying quantitatively or qualitatively a portion of the extracted RNA or cDNA therefrom to produce an amplified product, using primers or probes specific for a human RNA species or cDNA therefrom (ie., myc), and detecting quantitatively or qualitatively the amplified product as recited in claim 1

wherein the human RNA species is a tumor related RNA (ie., myc RNA) as recited in claim 4 (see pages 4 and 14-24).

Regarding claims 5 and 8, Balazs *et al.,* teach extracting total extracellular RNA from a non-cellular fraction of blood from a human (ie., a cancer patient), amplifying or signal amplifying quantitatively or qualitatively a portion of the extracted RNA or cDNA therefrom to produce an amplified product or signal, using primers or probes or detectably-labeled primers or detectably-labeled probes specific for a human RNA species or cDNA therefrom (ie., myc), and detecting quantitatively or qualitatively the amplified product or signal as recited in claim 5 wherein the human RNA species is a tumor associated RNA (ie., myc RNA) as recited in claim 8 (see pages 4 and 14-24).

Regarding claims 9, 12, and 45, Balazs *et al.,* teach extracting total extracellular RNA from plasma or serum from a human (ie., a cancer patient), a portion of which comprises a human RNA species and determining an amount or concentration of said human RNA species in the extracted portion of human blood plasma or serum as recited in claim 9 wherein the human has cancer as recited in claim 12 and the human has cancer and the RNA species is a tumor-associated RNA (ie., myc RNA) as recited in claim 45 (see pages 4 and 14-24).

Regarding claims 20, 23, and 46, Balazs *et al.,* teach extracting total extracellular RNA from a non-cellular fraction of blood from a human (ie., a cancer patient), a portion of which comprises a human RNA species and determining an amount or concentration of said human RNA species in the extracted portion of a non-cellular fraction of blood from a human as recited in claim 20 wherein the human has cancer as recited in claim 23 and the human has cancer and

the RNA species is a tumor-associated RNA (ie., myc RNA) as recited in claim 46 (see pages 4 and 14-24).

Balazs *et al.,* do not disclose comparing the detected amplified product to a reference amplified product of said human RNA species or cDNA extracted from plasma or serum from a human group or population without disease wherein the human RNA species extracted from human blood plasma or serum is determined to be overexpressed when the detected amplified product from the human in an amount or concentration greater than the reference amount or concentration of said RNA species or cDNA therefrom extracted from said blood plasma or serum from said human group or population without disease as recited in claim 1, comparing the detected amplified product or signal to a reference amplified product or signal of said human RNA species or cDNA extracted from a non-cellular fraction of blood from a human group or population without disease wherein the human RNA species extracted from a non-cellular fraction of blood is determined to be overexpressed when the detected amplified product or signal from the human in an amount or concentration greater than the reference amount or concentration of said RNA species or cDNA therefrom extracted from said non-cellular fraction of blood from said human group or population without disease as recited in claim 5, and comparing the amount or concentration of said human RNA species from plasma or serum of said human to the reference range RNA amount or concentration for said RNA species determined from plasma or serum from a human group or population without cancer as recited in claim 9, and comparing the amount or concentration of said human RNA species from a non-cellular fraction of blood of said human to the reference range RNA amount

or concentration for said RNA species from plasma or serum from a human group or population without cancer as recited in claim 20.

Guin *et al.*, teach to detect RNA including mRNA in blood plasma of healthy individuals (see page 224, last paragraph and page 228).

Korneluk *et al.,* teach to detect expression of hiap-1 in the Raji Burkitt's lymphoma cell line using RT-PCR and determine overexpression of hiap-1 by comparing with positive and negative controls (see column 26).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 1 or 5 or 9 or 20 by comparing the detected amplified product to a reference amplified product of said human RNA species or cDNA extracted from plasma or serum from a human group or population without disease wherein the human RNA species extracted from human blood plasma or serum is determined to be overexpressed when the detected amplified product or signal from the human in an amount or concentration greater than the reference amount or concentration of said RNA species or cDNA therefrom extracted from said blood plasma or serum from said human group or population without disease or by comparing the detected amplified product or signal to a reference amplified product or signal of said human RNA species or cDNA extracted from a non-cellular fraction of blood from a human group or population without disease wherein the human RNA species extracted from a non-cellular fraction of blood is determined to be overexpressed when the detected amplified product or signal from the human in an amount or concentration greater than the reference amount or concentration of said RNA species or cDNA therefrom extracted from a non-cellular fraction of blood from a human group or population

without said disease or by comparing the amount or concentration of said human RNA species from plasma or serum of said human to the reference range RNA amount or concentration for said RNA species determined from said plasma or serum from said human group or population without cancer or by comparing the amount or concentration of said human RNA species from a non-cellular fraction of blood of said human to the reference range RNA amount or concentration for said RNA species determined from said plasma or serum from said human group or population without cancer in view of the prior arts of Balazs *et al.,* Guin *et al*., and Korneluk *et al.*. One having ordinary skill in the art would have been motivated to do so because Guin *et al*., have shown to detect RNA including mRNA in blood plasma of healthy individuals (see page 224, last paragraph and page 228), Korneluk *et al.,* have shown to detect expression of hiap-1 in the Raji Burkitt's lymphoma cell line using RT-PCR and determine overexpression of hiap-1 by comparing with positive and negative controls (see column 26) and use of a reference amplified product or signal of said human RNA species or cDNA extracted determined from plasma or serum from a human group or population without disease as an experimental control or the use of a reference amplified product or signal of said human RNA species or cDNA extracted from a non-cellular fraction of blood from a human group or population without disease as an experimental control or the use of the reference range RNA amount or concentration for said RNA species determined from plasma or serum from a human group or population without cancer as an experimental control or the use of the reference range RNA amount or concentration for said RNA species determined from plasma or serum from a human group or population without cancer as an experimental control during the process of performing the method recited in claim 1 or 5 or 9 or 20, in the absence of convincing evidence to the

contrary, would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the experimental controls are needed to eliminate alternate explanations of experimental results and used to prevent the effects of one variable from being drowned out by the known, greater effects of other variables. One having ordinary skill in the art at the time the invention was made would have a reasonable expectation of success to perform the method recited in claim 1 or 5 or 9 or 20 by using a reference amplified product of said human RNA species or cDNA extracted from plasma or serum from a human group or population without disease as an experimental control or using a reference amplified product or signal of said human RNA species or cDNA extracted from a non-cellular fraction of blood from a human group or population without disease as an experimental control or using the reference range RNA amount or concentration for said RNA species determined from plasma or serum from a human group or population without cancer as an experimental control or using the reference range RNA amount or concentration for said RNA species determined from plasma or serum from a human group or population without cancer as an experimental control in order to eliminate alternate explanations of experimental results and prevent the effects of one variable from being drowned out by the known, greater effects of other variables.

8. Claims 14 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balazs *et al.,* in view of Guin *et al*., and Korneluk *et al.,* as applied to claims 1, 4, 5, 8, 9, 12, 20, 23, 45, and 46 above.

The teachings of Balazs *et al.,* Guin *et al.,* and Korneluk *et al.,* have been summarized previously, *supra*.

Balazs *et al.,* Guin *et al.,* and Korneluk *et al.,* do not disclose that the human is a human who has not been diagnosed with cancer as recited in claims 14 and 25. However, Guin *et al.,* teach that said human group or population is a human group or population without cancer as recited in claims 9 and 20 (ie., healthy individuals) (see page 224, last paragraph and page 228).

However, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 9 or 20 using a human who has not been diagnosed with cancer as recited in claim 14 or 25 in view of prior art of Balazs *et al.,* Guin *et al.,* and Korneluk *et al.*. One having ordinary skill in the art would have been motivated to do so because use of the plasma or serum or non-cellular fraction from a different human for performing the method recited in claim 9 or 20, in the absence of convincing evidence to the contrary, would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

9. Claims 17, 18, 28, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balazs *et al.,* in view of Guin *et al.,* and Korneluk *et al.,* as applied to claims 1, 4, 5, 8, 9, 12, 20, 23, 45, and 46 above.

The teachings of Balazs *et al.,* Guin *et al.,* and Korneluk *et al.,* have been summarized previously, *supra*.

Balazs *et al.,* and Korneluk *et al.,* do not disclose that the group or population comprises humans of a specific sex or age group as recited in claims 17 and 28 and the group or population comprises humans who smoke as recited in claims 18 and 29. However, Guin *et al.,* teach that the group or population comprises humans of a specific age group (ie., ages 3-62) as recited in claims 17 and 28 (see page 224, last paragraph and page 228)

However, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 9 or 20 using the group or population comprising humans of a specific sex or age group as experimental controls as recited in claim 17 or 28 or using the group or population comprises humans who smoke as experimental controls as recited in claim 18 or 29 in view of prior art of Balazs *et al.,* Guin *et al.,* and Korneluk *et al.*. One having ordinary skill in the art would have been motivated to do so because use of the plasma or serum or non-cellular fraction from a different group or population as an experimental control for performing the method recited in claim 9 or 20, in the absence of convincing evidence to the contrary, would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their

expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. No claim is allowed.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30

(November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached on (571)272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Frank W Lu /
Primary Examiner, Art Unit 1634
December 22, 2009